الجامعة التقنية الوسطى

كلية التقنيات الصحية والطبية /بغداد

قسم تقنيات التحليلات المرضية

المادة: فايروسات

المرحلة:- الثالثة

## Title:-

# Paramyxoviruses

**Lecture 11**

## Name of the instructor:

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## Target population

**Three stage students in department Medical Laboratory Techniques**

## Introduction

The paramyxoviruses include the most important agents of respiratory infections of infants and young children (respiratory syncytial virus [RSV] and the parainfluenza viruses) as well as the causative agents of two of the most common contagious diseases of childhood (mumps and measles). The World Health Organization estimates that acute respiratory infections and pneumonia are responsible every year worldwide for the deaths of 4 million children younger than 5 years. Paramyxoviruses are the major respiratory pathogens in this age group.

All members of the **Paramyxoviridae** family initiate infection via the respiratory tract. Whereas replication of the respiratory pathogens is limited to the respiratory epithelia, measles and mumps become disseminated throughout the body and produce generalized disease.

**Classification**

The family Paramyxoviridae consists of three important genera

1- Paramyxovirus includes parainfluenza and mumps virus.

2- Morbillivirus includes the measles virus.

**3-**Pneumovirus includes respiratory syncytial virus (RSV), which is responsible for majority of acute respiratory infections in infants and children

**PARAMYXOVIRUS FAMILY**

| GENUS | MEMBERS | GLYCOPROTEINS |
|---|---|---|
| Paramyxovirus | mumps<br>human parainfluenza viruses (HPIV 1-4) | HN, F |
| Morbillivirus | Measles | H, F |
| Pneumovirus | Respiratory syncytial virus | G, F |

## Pre-test

**Which the following of paramyxoviruses belong to pneumovirus ?**

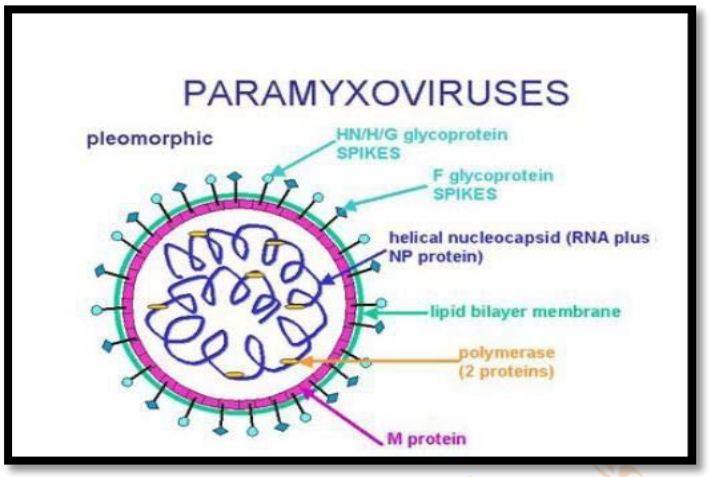
measles virus, parainfluenza , mumps virus , respiratory syncytial virus (RSV)

## Scientific Content

**Properties of Paramyxo viruses**

- **Virion:**Spherical,pleomorphic,150 nm or more in diameter (helicalnucleocapsid,13–18nm)
- **Composition:** RNA(1%),protein (73%),lipid (20%), carbohydrate(6%)
- **Genome:** Single- stranded negative RNA, linear,non segmented ,about15kb, no reassortment .
- **Proteins:** Six to eight structural proteins.
- **Envelope:** Contains viral glycoprotein(G ,H, or HN)(which sometimes carries hemagglutinin or neuraminidase activity) and fusion(F) glycoprotein
- **Replication:** Cytoplasm ; particles bud from plasma membrane. . A large excess of nucleocapsids are produced in infected cells, which form characteristic cytoplasmic inclusion bodies.
- **Outstanding characteristics :** Antigenically stable Particles are labile yet highly infectious.

**Transmission :-** spread by droplets from the nose and mouth to close contacts. Many of them are highly infectious and go around the community in epidemics- often seasonal, eg. Winter coughs and colds. Fomites might also assist spread.




**Structure of Paramyxovirus**

### ♦ Human parainfluenza viruses (HPIVs)

HPIVs are single-stranded, enveloped RNA viruses of the Paramyxoviridae family. There are four serotypes(1-4) which cause respiratory illnesses in children and adults. HPIVs bind and replicate in the ciliated epithelial cells of the upper and lower respiratory tract and the extent of the infection correlates with the location involved. Seasonal HPIV epidemics result in a significant burden of disease in children and account for 40% of pediatric hospitalizations for lower respiratory tract illnesses and **75% of croup cases.**

### Pathogenesis of human parainfluenza virus (HPIV) infection

The virus adsorbs to the respiratory epithelial cells by specifically combining with neuraminic acid receptors in the cell through its hemagglutinin. Subsequently, the virus enters the cells following fusion with the cell membrane, mediated by F1 and F2 receptors. The virus replicates rapidly in the cell cytoplasm and causes formation of multinucleated giant cells. The virus also causes the formation of single and multilocular cytoplasmic vacuoles and basophilic or eosinophilic inclusions.

The virus causes inflammation of the respiratory tract, leading to secretions of high level of inflammatory cytokines, usually 7–10 days after initial exposure. Airways inflammation, necrosis, and sloughing of respiratory epithelium, edema, and excessive mucus production are the noted pathological features associated with HPIV infections.

**Clinical feature**

Human parainfluenza viruses cause **croup** (a heterogeneous group of illnesses that affects the larynx, trachea, and bronchi. The condition manifests as fever, cough, laryngeal obstruction), pneumonia, bronchiolitis and tracheobronchitis, and Otitis media, pharyngitis, conjunctivitis. The severity of the disease occurred in infant less than 6 months.

- **Laboratory Diagnosis**
- **Clinical feature**
- **Respiratory specimens** include nasopharyngeal aspirations nasal washings, and nasal aspirations.

**1- Direct antigen detection**

The ELISA, immunofluorescence assay are used to detect HPIV antigen

**2-Molecular Diagnosis :**

polymerase chain reaction (PCR) has been developed for detection of HPIV-1, HPIV-2, and HPIV-3 genome in clinical specimens.

**3- Isolation and identification**

Nasal wash are good specimens, culture in monkey kidney cell line , the diagnosis depending on hem adsorption

- **Prevention and Control**

Currently there is no vaccine against infection by HPIV, However, researchers are trying to develop one.

**Mumps**

Mumps is an acute contagious disease characterized by nonsuppurative enlargement of one or both salivary glands. Mumps virus mostly causes a mild childhood disease, but in adults complications including meningitis and orchitis are fairly common. More than one-third of all mumps infections are asymptomatic.

**Pathogenesis & Pathology**

Humans are the only natural hosts for mumps virus. Primary replication occurs in nasal or upper respiratory tract epithelial cells.

Viremia then disseminates the virus to the salivary glands and other major organ systems. Involvement of the parotid gland is not an obligatory step in the infectious process. The incubation period may range from 2 to 4 weeks but is typically about 14–18 days. Virus is shed in the saliva from about 3 days before to 9 days after the onset of salivary gland swelling. About one-third of infected individuals do not exhibit obvious

symptoms (in apparent infections) but are equally capable of transmitting infection. Virus frequently infects the kidneys and can be detected in the urine of most patients. Viruria may persist for up to 14 days after the onset of clinical symptoms. The central nervous system is also commonly infected and may be involved in the absence of parotitis.

**Clinical Findings**

Fever, malaise followed by rapid enlargement of the parotid gland and it is painful . mumps may be associated with aseptic meningitis . testis and ovaries may be infected especially after puberty and it may pass to sterility in man but it is rare ( not more than 1%).

**Laboratory diagnosis of Mumps virus**

**1) Clinical feature**

**2) Isolation and identification**

The most appropriate clinical samples for viral isolation are saliva, cerebrospinal fluid, and urine collected within a few days after onset of illness. Virus can be recovered from the Culture in monkey kidney cells urine for up to 2 weeks**.**
and diagnosis by using mumps specific antiserum by immunofluorescence method, hemadsorption test can also be used.

**3) Nucleic acid detection**:- by PCR test.

**4) Serology**

IgM and IgG Abs detection by ELISA and Heamagglution inhibition test.

**Treatment , Prevention**

- There is no specific therapy .
- Immunization with attenuated live mumps virus vaccine is the best approach to reducing mumps-associated morbidity and mortality rates. Mumps vaccine is available in combination with measles and rubella (MMR) live-virus vaccines.

**Measles**

Measles is an acute, highly infectious disease characterized by fever, respiratory symptoms, and a maculopapular rash. Complications are common and may be quite serious.

**Pathogenesis & Pathology**

Humans are the only natural hosts for measles virus. The virus gains access to the human body via the respiratory tract, where it multiplies locally; the infection then spreads to the regional lymphoid tissue, where further multiplication occurs. Primary viremia disseminates the virus. Finally, a secondary viremia seeds the epithelial surfaces of the body, including the skin, respiratory tract, and conjunctiva, where focal replication occurs. The described events occur during the incubation period, which typically lasts 8–12 days but may last up to 3 weeks in adults. involvement of the central nervous system is common in measles.

**Clinical Findings**

Infections in non immune hosts are almost always symptomatic. After an incubation period of 8–12 days, measles is typically a 7-11days illness. The prodromal phase is characterized by fever, sneezing, coughing, running nose, redness of the eyes, **Koplik spots**, and lymphopenia. The conjunctivitis is commonly associated with photophobia. **Koplik spots** are small, bluish-white ulcerations on the buccal mucosa opposite the lower molars. These spots contain giant cells and viral antigens and appear about 2 days before the maculopapular rash. . The most common complication of measles is **otitis media** (5–9% of cases**). Pneumonia** is the most common life-threatening complication of measles, caused by secondary bacterial infections.

**Subacute sclerosing panencephalitis (SSPE)** is a very rare, but fatal disease of the central nervous system that results from **a measles virus infection** acquired earlier in life SSPE generally develops 7 to 10 years after a person has measles**.**

**Laboratory Diagnosis**

**1) Clinical feature**

**2) Isolation & Identification of Virus**

● Nasopharyngeal and conjunctival swabs, blood samples, respiratory secretions, and urine collected from a patient during the febrile period are appropriate sources for viral isolation. culture in monkey and human kidney cells , diagnosis by cytopathic effect , multinucleated and intra nuclear and intra cytoplasmic inclusion bodies.

**3- Antigen detection**

Measles antigen can be directly detected from specimen include respiratory secretion , nasopharynx and conjunctiva by Immunofluorescence test.

**4- Serology**

IgM and IgG antibodies by ELISA and Heamagglution inhibition test (HI) test.

**5- Detection of viral RNA by RT-PCR**

Is a sensitive method that can be applied to a variety of clinical samples for measles diagnosis.

**Treatment, Prevention, & Control**

No treatment . A highly effective and safe attenuated live measles virus vaccine has been available since 1963.

**Respiratory syncytial virus(RSV)**

It is the most common cause of lower respiratory tract illness in infant and young children.

**Pathogenesis and pathology**

Replication of the virus occurred initially in the nasopharynx , then the virus may spread to the lower respiratory tract and produce bronchiolitis and pneumonia. The incubation period 3-5 days and virus shedding for 1-3 weeks.

**Clinical findings :-**

Common cold , pneumonia in infant and may bronchitis and bronchiolitis which Life-threatening disease in infant especially under 6, and can lead to chronic lung disease in later life. Reinfection is common in both children and adult with less severity. This virus are a common cause of otitis media about 30% of otitis media cause in infant .

**Laboratory diagnosis of Respiratory syncytial virus (RSV)**

**1- Clinical feature**

**2- Antigen detection**

Nasal wash or aspirate are good sample .Virus antigens detection by immunofluorescence test .

**3- Isolation and identification of the virus**

By culturing the specimen into human heteroploid cell line ( Hela) and Hep-2, the diagnosis is depend on the cytopathic effect and appearance of giant cells.

**4- Nucleic acid detection**

Diagnosis by detection of the RNA of the virus by PCR.

**5-Serology**

Detection of serum antibodies which include IgM and IgG Abs by using immunofluorescence test .

## Treatment

Supportive care , Ribavirin may be used in the treatment of severe cases by aerosol for 3-6 days . No vaccine is available today but passive immunization immunoglobulin can be given for infected premature infants.

## Post test

**Q :- Multiple choice :-**

**1- Croup caused by :-**

a- Measles virus b- Mumps virus c- RSV d- Parainfluenza virus

**2- Koplik spots occur in :-**

a- Mumps b- RSV c- Measles d- Parainfluenza virus

3- **SSPE** is complication of :-

a- Parainfluenza virus b- Measles c- Mumps d- RSV

**4- Orchitis caused by :-**

a- Measles virus b- RSV c- Mumps virus d- Parainfluenza virus

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## Title:-

# Enteric viruses ( Polio, Rota) Lecture 12

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## Target population

Three stage students in department Medical Laboratory Techniques

## Introduction

**Enteric viruses** represent a wide spectrum of viral genera that invade and replicate in the mucosa of the intestinal tract .Enteric viruses are the commonest causes of gastroenteritis worldwide, they are most often transmitted via the fecal-oral route, with transmission by direct human contact and via fomites being common. Enteric viruses may also be present in contaminated water supplies.Enteric viruses can be grouped as follows:

**1)** Viruses causing localized inflammation at any level of the intestinal tract, predominantly in small intestinal mucosa, resulting in acute gastroenteritis, for example, rotaviruses, caliciviruses, adenoviruses, astroviruses .

**2)** Viruses that multiply at any level of the intestinal tract, causing few enteric symptoms prior to producing clinical disease at a distant site, for example, measles virus, reoviruses , enteroviruses (including polioviruses, coxsackieviruses, hepatitis A and E).

**3)** Viruses that spread to the intestinal tract during the later stages of systemic disease, generally in an immunocompromised host, for example, human immunodeficiency virus (HIV), cytomegalovirus.

**Pre-test**

**Define Enteric Viruses ?**

# Scientific Content

## Polio Virus

Polio virus is the causative agent of polio (also known as poliomyelitis) which is a highly contagious disease caused by a virus that attacks the central nervous system. Children younger than 5 years old are more likely to contract the virus than any other group **.**

### Structure and properties of polio Virus

1- Virus classification : Picornaviridae ,Genus Enteroviruses .
2- Virion :- Viral particle is spherical in shape about 30 nm in diameter with icosahedral symmetry .
3- Genome :- is a single-stranded positive-sense RNA (+ssRNA) , linear with 7500 nucleotides long .
4- The particles are simple in that they are composed of **a protein shell** surrounding the **naked RNA genome**.
5- The virus particles **lack a lipid envelope**, and their infectivity is insensitive to organic solvents.
**5-** Humans are the only susceptible hosts.
**6-** Three serotypes of poliovirus, PV-1, PV-2, and PV-3.
**7- Capsid** contains 60 copies each of the four viral polypeptides VP1, VP2, VP3, and VP4.
**8-** Replication of Polio Virus occur in the **cytoplasm** . viral particles are release from the host cell through **lysis** of the cell.

### Pathogenesis of Polio Virus

The mouth is the portal of entry for the virus, transmitted by fecal oral route on ingestion of contaminated water. **The incubation period is 9-12 days.**
Following ingestion, the virus multiplies in the oropharyngeal and intestinal mucosa. The lymphatic system , in particular the tonsils and the Peyer's patches of the ileum are invaded and the virus enters the blood resulting in primary viraemia . Antibodies to the virus appear early in the disease, usually before paralysis occurs. The antibodies are produced to prevent infection from spreading. In a minority of cases, On continued

infection and multiplication of virus in the ReticuloEndothelial System (RES), it invades the blood stream causing secondary viremia **.** During this period of viremia, the poliovirus crosses the blood brain barrier and gain access to the brain. The virus shows tissue tropism by specifically combining with neural cells. The virus recognizes the receptor present on the anterior horn of spinal cord, dorsal root ganglia and motor neurons. The destruction of motor neurons leads to paralysis.

**Clinical Manifestations of Polio Virus**

There are 3 possible outcomes of infection:

**1- Subclinical infection (90 - 95%) :** – in apparent subclinical infection account for the vast majority of poliovirus infections.

**2- Abortive infection (4 - 8%) :-** a minor influenza-like illness occurs characterized by fever, headache, sore throat, loss of appetite, vomiting, and abdominal pain. **Neurological symptoms are typically absent.**

**3- Major illness (1-2%)** :- the major illness may present 2 - 3 days following the minor illness or without any preceding minor illness. Signs of aseptic meningitis are common. Involvement of the anterior horn cells of spinal cord lead to flaccid paralysis. Involvement of the medulla may lead to respiratory paralysis and death.

**Laboratory Diagnosis of Polio Virus**

**Specimen:**

Stool, rectal swab, throat swab, CSF (rare)

**1- Microscopy**

Virus can be detected in stool specimens by direct electron microscopy or also by immune electron microscopy.

**2- Virus isolation**

Virus may be recovered from pharyangeal aspirations and feces. Virus isolation from feces and throat swab is carried out by cultivation on monkey kidney, human amnion, HeLa cells, Hep-2 and other cell cultures. Cytopathogenic effects appear in 3–6 days. An isolated virus is identified and typed by neutralization with specific antiserum .

**3-Serodiagnosis**

Demonstration of antibody titer in the serum sample collected at the time of acute illness and time of convalescence. **Neutralization test** and **complement fixation** test is carried out to demonstrate antibodies presence.

**Treatment of Polio Virus**
No antiviral treatments are available for the treatment of poliomyelitis.

**Prevention**
The disease may be prevented through Vaccination. There are two vaccines available :-
**1- Intramuscular Poliovirus Vaccine (IPV)**:- consists of formalin inactivated virus of all 3 poliovirus serotypes. Produces serum antibodies only: does not induce local immunity and thus will not prevent local infection of the gut.

**2- Oral Poliovirus Vaccine (OPV)**
Consists of live attenuated virus of all 3 serotypes. Produces local immunity through the induction of an IgA response as well as systemic immunity.

## Rotavirus

### ► Classification of Rotavirus:

- Family: **Reoviridae**
- Genus: **Rotavirus**
- Classified into seven distinct groups (A to G) based on structural antigen VP6.

Group A, B, and C Rotaviruses are found in Human infection as well as animal infection. Group A Rotaviruses are most frequent Human pathogen.

### ► Structure, composition and properties of Rotavirus

- Characteristics **"wheel"** like appearance (Rota-means wheel).
- **Size:** 65nm-100nm in diameter.
- **Shape:** Spherical shape.
- **Symmetry:** Icosahedral.
- **Genome:** 11 segments of **double stranded RNA (ds RNA** ).
- **Protein:** 6 structural protein (VP) and 6 Non-structural protein (NSP).
- **Envelope:** Absent

Nucleic acid is surrounded by two layer of capsid- **inner capsid (VP6)** and **outer capsid (VP7)**.
**VP4** is the spike protein, it is a cell surface receptor.
**Replication:** Occurs in cytoplasm of infected cell.
Rota virus contain an **RNA-dependent RNA polymerase** and other enzymes capable of producing capped RNA transcripts.
Rota virus do not **grow in cell line culture**.

## ► Mode of Transmission:

- Ingestion of contaminated food and water.
- Directly from faces contaminated fingers.
- Occasionally by droplet infection.
- Children below 5 years are mostly affected.
- Adults are infected by contact with pediatric cases.

## ► Pathogenesis:

Incubation period: 2-3 days

● Rota virus replicates in enterocyte near the tip of villi destroying enterocytes.

● Viral encoded toxin: early profuse, secretory diarrhea is caused by enterotoxin, NSP4.

● Disruption of intestinal epithelium due to virus replication

● Histologic changes of enterocytes that triggers enteric nervous system, intestinal secretion and immune response.

● The acute infection and diarrhea normally resolves within 7 days in immunocompetent hosts.

## Clinical symptoms:

### 1- Local infection:

● Acute Gastroenteritis, severe in case of infants aged 6-24 months.

●Infected Infants are unable to digest milk due to lactase deficiency caused by destruction of enterocytes

● Diarrhea, nausea and vomiting

● Malabsorption of Na+, water and disaccharides.

● Symptoms of Dehydration: decrease in urination, dry mouth and throat and feeling dizzy when standing up.

### 2. Systemic infection:

High grade Fever

Lymphocytosis and transient neutropenia.

### Laboratory diagnosis:

Specimen: faces in early infection,

**1- Viral antigen detection:** by solid phase agglutination , ELISA (it is sensitive for detected virus in stool sample , Electron microscopy.

**2-PCR:** For genotyping of Rotavirus.

**3-Virus culture**: No cell line culture.

**Treatment:**

- Oral rehydration
- Other supportive rehydration therapy to control loss of water and electrolytes.

Vaccine: Two Oral rotavirus vaccines are currently licensed for use in infants:-
1- RotaTeq (RV5) is given in 3 doses at ages 2 months, 4 months, and 6 months.
2- Rotarix (RV1) is given in 2 doses at ages 2 months and 4 months.

## Post test

Q1:- Mention Clinical Manifestations of Polio Virus?
Q2 :- Answer True or false
1- Polio virus contain envelope membrane.
2- Group C Rotaviruses are most frequent Human pathogen.

## References

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2- Jawetz, R., J.L. Melnick, and E.A. Adelberg,( 2019). Review of Medical Microbiology, Twenty-Eighth Edition Edition,.

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## Title:-

**Rabies Virus** **Lecture 13**

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## Target population

**Three stage students in department Medical Laboratory Techniques**

## Introduction

The family Rhabdoviridae consists of more than 100 single-stranded, negative-sense, non segmented viruses that infect a wide variety of hosts, including vertebrates, invertebrates, and plants. Common to all members of the family is a distinctive **rod- or bullet-shaped** morphology. Human pathogens of medical importance are found in the genera Lyssavirus and Vesiculovirus.Only **rabies virus**, medically the most significant member of the genus Lyssavirus.

Rabies virus causes acute infection of the central nervous system .

### Pre-test

**Family of rabies virus called :-**

1- Retroviridae b- Rhabdoviridae c- Hepdnaviridae d- Reoviridae

## Scientific Content

► This virus transmitted by Zoonosis.

► Rabies virus is the most important member of the rhabdoviridae

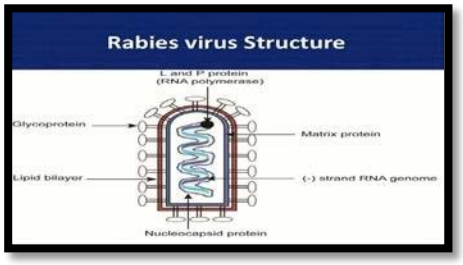
family, which causes disease in humans.

►This virus affects the central nervous system (cases inflammation in the brain ).
► Primary reservoirs are wild mammals; it can be spread by both wild and domestic mammals by bites, scratches, and inhalation of droplets

►Multiplication of the virus occurs in cytoplasm of infected cells , viral proteins together with the viral RNA aggregate in the cytoplasm of virus infected neurons and compose Negri bodies.

**Morphology:**

● Bullet – shaped virus, size (180-75nm),with one end rounded. Enveloped RNA virus .
● Genome :-, linear , negative-sense ,SS RNA virus, unsegmented.
● Host Range **:-** Animal: Domestic dogs, cats and wild animals.




● **Antigenic Properties:**

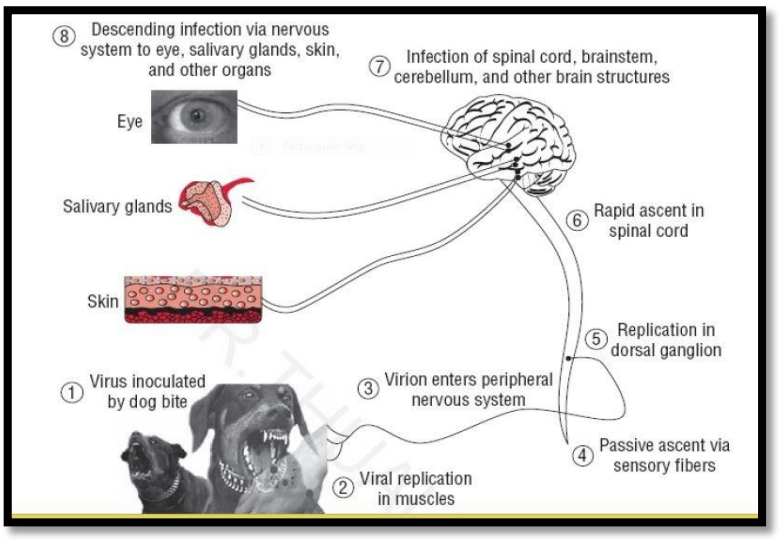
❖ **G protein:** The glycoprotein or G protein is present on the surface spikes present on the outer lipoprotein envelope of the virion, helps to absorb receptor on the nerve tissues.
❖ **N protein:** Nucleoprotein or N protein is a group-specific antigen. It shows cross-reaction with some rabies-related viruses.
❖ **Other antigens:** These include membrane proteins, glycolipid and RNA-dependent RNA polymerase
❖ Ab produce against these Ag-are protective.

## Pathogenesis:

● Human infection is usually caused by the bite of dogs or other animals.

● Virus present in the saliva of the animals also can caused by licks or aerosols.

Entry in the body
(once it is bites)
U
Rabies is virus deep inside the muscle (saliva).
U
Multiple in muscle tissue, connective tissue.
U
Reach nerve or neural cell
U
Finally reaches the brain and produce Negri bodies in human.




**Clinical Manifestations**

Five general stages of rabies are recognized in humans:

1- incubation period :- usually 30 to 90 days but ranging from as few as 5 days to longer than 2 years after initial exposure.

2- Prodromal period, which usually lasts from 2 to 10 days. These symptoms are often nonspecific include fever, nausea, vomiting, headache, fatigue, sore throat, cough.
3- Acute neurological period (2 to 3 days, rarely up to 6 days).
4- coma
5- death

**Lab Diagnosis:-**

► Specimen – saliva , CSF, Brain biopsy, skin biopsy, cornea.

1. Direct detection by Microscope (immunofluroscent staining technique ( for Ag detection).

2. Isolation of virus (cell lines, egg yolk, mice) to detect Negri bodies and viral Ag.

3- Detection of rabies virus-neutralizing antibody.

4- Molecular method for detection viral RNA.

**Treatment:**

No specific treatment for this virus .

**Prevention:**

By vaccination – Both active & passive

## Post test

## References

1- Review of Medical Microbiology and Immunology. Warren Levinson, 12th May 2012. Mc Graw-Hill (Lange).

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## Title:-

**Pox virus** **Lecture 14**

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## Target population

**Three stage students in department Medical Laboratory Techniques**

# Introduction

Poxviruses are the largest and most complex of viruses. Infections with most poxviruses are characterized by a rash, although lesions induced by some members of the family are markedly proliferative. The group includes variola virus, the etiologic agent of smallpox—the viral disease that has affected humans throughout recorded history.

## Pre-test

**Q :- Answer True or false :-**

1- Poxviruses are the smallest and most complex of viruses ?

# Scientific Content

### Properties of Poxviruses

- **Virion:** Complex structure, oval or brick-shaped, 400 nm in length x 230 nm in diameter; external surface shows ridges; contains core and lateral bodies.
- **Composition:** DNA (3%), protein (90%), lipid (5%).
- **Genome :** Double-stranded DNA, linear; size 130–375 kbp; has terminal loops; has low G + C content (30–40%) except for *Parapoxvirus* (63%).
- **Proteins:** Virions contain more than 100 polypeptides; many enzymes are present in core, including transcriptional system
- **Envelope:** Virion assembly involves formation of multiple membranes
- **Replication:** Cytoplasmic factories
- **Outstanding characteristics:**

→ Largest and most complex viruses; very resistant to inactivation .

→ Virus-encoded proteins help evade host immune defense system.

→ Smallpox was the first viral disease eradicated from the world.

### Classification

Poxviruses are divided into two subfamilies based on whether they infect vertebrate or insect hosts. The vertebrate poxviruses fall into eight genera, with the members of a

given genus displaying similar morphology and host range as well as some antigenic relatedness.

Most of the poxviruses that can cause disease in humans are contained in the genera Orthopoxvirus and Parapoxvirus .

**Poxvirus Replication**

Virus particles establish contact with the cell surface and fuse with the cell membrane. Viral cores are released into the cytoplasm. The mRNAs are transcribed within the viral core and are then released into the cytoplasm. The "uncoating" protein that acts on the cores is among the more than 50 polypeptides made early after infection. The second stage uncoating step liberates viral DNA from the cores; it requires both RNA and protein synthesis.

Viral DNA replication occurs in the cytoplasm and appears to be accomplished by viral coded enzymes. Viral DNA replication occurs 2–6 hours after infection in discrete areas of the cytoplasm.

Mature virions appear in electron micrographs as a DNAcontaining core encased in double membranes, surrounded by protein, and all enclosed within **two outer membranes**. Some of the particles are released from the cell by budding, but the majority of poxvirus particles remain within the host cell.

**Poxvirus Infections in Humans: Vaccinia and Variola.**

**Comparison of Vaccinia and Variola Viruses**

**Vaccinia virus**, the agent used for smallpox vaccination, is a distinct species of Orthopoxvirus.

**Variola** has a narrow host range (only humans and monkeys), whereas **vaccinia** has a broad host range that includes rabbits and mice. Some strains of vaccinia can cause a severe disease in laboratory rabbits that has been called rabbitpox. Vaccinia virus has also infected cattle and water buffalo, and the disease in buffalo (buffalopox). Both vaccinia and variola viruses grow on the chorioallantoic membrane of the 10- to 12-day-old chick embryo, but the latter produce much smaller pocks. Both grow in several types of chick and primate cell lines**.**

**Pathogenesis & Pathology of Smallpox**

The portal of entry of variola virus was the mucous membranes of the upper

respiratory tract. After viral entry, the following are believed to have taken place: (1) primary multiplication in the lymphoid tissue draining the site of entry; (2) transient viremia and infection of reticuloendothelial cells throughout the body; (3) a secondary phase of multiplication in those cells, leading to (4) a secondary, more intense viremia; and (5) the clinical disease.

By the sixth to ninth days, lesions in the mouth tended to ulcerate and discharge virus. Later, pustules broke down and discharged virus into the environment of the smallpox patient.

**Clinical Findings**

The incubation period of variola (smallpox) was 10–14 days. The onset was usually sudden. One to 5 days of fever and malaise preceded the appearance of the exanthems, which began as macules, then papules, then vesicles, and finally pustules. These formed crusts that fell off after about 2 weeks, leaving pink scars that faded slowly.

**Immunity**

An attack of smallpox gave complete protection against reinfection. Vaccination with vaccinia induced immunity against variola virus for at least 5 years and sometimes longer.

**Laboratory Diagnosis**

Several tests are available to confirm the diagnosis of smallpox.

1- **Isolation and Identification of Virus**

Skin lesions are the specimen of choice for viral isolation.

2- **Serology**

Antibody assays can be used to confirm a diagnosis.

**Treatment**

**Vaccinia** immune globulin is prepared from blood from persons vaccinated with the vaccinia virus. **Methisazone** is a chemotherapeutic agent of some value against poxviruses.

**Time of Vaccination**

Complications of vaccination occur most commonly under the age of 1 year. Therefore, vaccinating between 1 and 2 years of age is preferable to vaccinating in the first year of life. Revaccination has been done at 3-year intervals.

**Post test**

## References

1- Review of Medical Microbiology and Immunology. Warren Levinson, 12th May 2012. Mc Graw-Hill (Lange).

2- Jawetz, R., J.L. Melnick, and E.A. Adelberg,( 2019). Review of Medical Microbiology, Twenty-Eighth Edition Edition,.

## Title:-

**Coronaviruses** **Lecture 15**

## Name of the instructor:

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## Target population

**Three stage students in department Medical Laboratory Techniques**

## Introduction

Coronaviruses are large a family of viruses , enveloped RNA viruses and they are called “corona” because of crown-like spikes on the surface of the virus . Coronaviruses are known to cause disease in humans, other mammals, and birds. In humans coronaviruses cause common colds, may cause lower respiratory tract infections and have been implicated in gastroenteritis in infants. Novel coronaviruses have been identified as the cause of severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) and the new strain of coronavirus — SARS-CoV-2 — was first reported in Wuhan, China in December 2019. It has since spread to every country around the world.

The human viruses are difficult to culture and therefore are more poorly characterized.

### Pre-test

**Q :- Mention strains of coronavirus that cause diseases in human ?**

### Scientific Content

Important properties of coronaviruses

►**Virion :-** Spherical, 120-160 nm in diameter, helical nucleocapsid

►Genome:- Single-stranded RNA linear, non segmented , positive-sense,27-32kb, infectious.

►**Protein :-** virions contain three or four structural proteins: a major spike glycoprotein (S), trans membrane glycoproteins (M and E), a nucleoprotein (N), and in some viruses, a hemagglutinin esterase (HE).

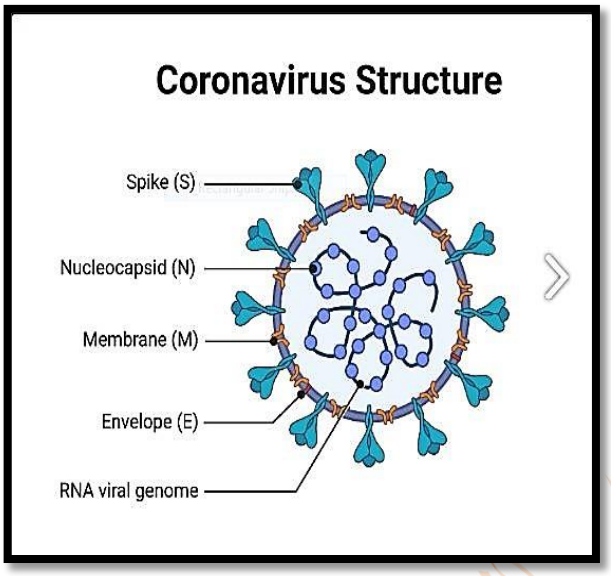
►Envelope :- contain large ,widely spaced, club-shaped spikes.

► Replication :- in cytoplasm, particles mature by budding into endoplsmic reticulum and Golgi apparatus .

►Outstanding characteristic:-

- Cause colds and SARS
- Display high frequency of recombination

- Difficult grow in cell culture




**Classification**

Coronaviruses belong to the family Coronaviridae ,subfamily Coronarivinae , and order Nidovirales were classified depend on the basis of the crown or halo-like appearance of the envelope glycoproteins and on characteristic features of chemistry and replication .

Depending on the serotype they are divided in 4 genera: α, β, γ and δ-CoVs. α and β-CoVs infect human and γ and δ-CoVs infect birds . Seven serotypes infect the human: 229E, NL63 (α-CoVs); OC43, HKU1 (β-CoVs, lineage A); SARS (β-CoV, lineage B); MERS (β-CoV, lineage C) and the most recent SARS-CoV-2 (β-CoV, lineage B).

## Coronavirus Replication

The entire cycle of coronavirus replication occurs in the cytoplasm.

The virus attaches to receptors on target cells by the glycoprotein spikes on the viral envelope (either by S or HE). The receptor for human coronavirus 229E is aminopeptidase N, whereas a functional receptor for the SARS virus is **angiotensin-converting enzyme 2.**

after uncoating translation of the viral genomic RNA to produce a virus-specific RNA-dependent RNA polymerase.The viral polymerase transcribes a full length complementary (minus-strand) RNA. which are used to synthesize full-length genomic RNA and subgenomic mRNA. new virions form by budding from host cell membranes.

**Transmission:**

The virus is usually transmitted vi**a inhalation of contaminated droplets**, but it may also be **transmitted by the hands to the mucosa of the nose or eyes** . also **contaminated surfaces and fomites.**

**Clinical Findings**

♦ The human coronaviruses produce "colds," usually a febrile in adults. The symptoms are similar to those produced by rhinoviruses, typified by nasal discharge and malaise. The incubation period is from 2 to 5 days.

♦ The SARS coronavirus causes severe respiratory disease. The incubation period averages about 6 days. Common early symptoms include fever, malaise, chills, headache, dizziness, cough, and sore throat, followed a few days later by shortness of breath and may lead to pneumonia and death rate highest among the elderly from progressive respiratory failure occurs in almost 10% of cases.

**Pathogenesis**

Transmission is usually via airborne droplets to the nasal mucosa.Virus replicates locally in cells of the ciliated epithelium. Infected cells become vacuolated, show damaged cilia, and may form syncytia . Cell damage triggers the production of inflammatory mediators, which increase nasal secretion and cause local inflammation and swelling. These responses in turn stimulate sneezing, obstruct the airway, and raise the temperature of the mucosa.

**Laboratory Diagnosis**

**- Specimens:-** Nasopharyngeal swabs, throat swab, saliva, other lower respiratory tract secretions, blood , stool.

**A. Antigen and Nucleic Acid Detection**

● Coronavirus antigens in cells in respiratory secretions may be detected using the **ELISA test** if a high-quality antiserum is available.

● Enteric coronaviruses can be detected by examination of stool samples by electron microscopy.**Polymerase chain reaction (PCR) assays** are useful to detect coronavirus nucleic acid in respiratory secretions and in stool samples.

- **Virus RNA** was detectable in plasma by **PCR** with viremia most readily detectable between days 4 and 8 of infection.

**B. Serology**

Because of the difficulty of virus isolation, serodiagnosis using acute and convalescent sera is the practical means of confirming coronavirus infections. ELISA, indirect immunofluorescent antibody assays, and hemagglutination tests may be used.

**C. Computed tomography (CT)** examination is plays an important role in the diagnosis of SARS-CoV-2 pneumonia .

**Treatment**

The treatment of coronavirus colds remains symptomatic. No specific treatment for SARS-CoV-2 . most people with mild COVID-19, rest and drinking plenty of fluids are the best approach. severe cases require hospital care, including breathing support, mechanical ventilation, or other medical treatments. The transmission can be reduced by practicing hygienic measures.

## Post test

**Q1 :- Multiple Choice :-**

**1- Receptor for the SARS virus is :-**

a- Aminopeptidase N b- angiotensin-converting enzyme c- hemagglutinin esterase d- Non of them

**2- Genome of Coronavirus belong to the:-**

a- ss RNA negative sense b- ds DNA c- ss RNA positive sense d- ds RNA

**Q2 :-Mention strains or serotypes of coronavirus that cause diseases in human?**

## References

1- Review of Medical Microbiology and Immunology. Warren Levinson, 12th May 2012. Mc Graw-Hill (Lange).

2- Jawetz, R., J.L. Melnick, and E.A. Adelberg,( 2019). Review of Medical Microbiology, Twenty-Eighth Edition Edition,.

3- Christopher J. Burrell, ... Frederick A. Murphy, in Fenner and White's Medical Virology (Fifth Edition), 2017

الجامعة التقنية الوسطى

كلية التقنيات الصحية والطبية /بغداد

قسم تقنيات التحليلات المرضية المادة: فايروسات المرحلة:- الثالثة

## Title:-

# Adenovirus and Parvovirus Lecture 16

## Name of the instructor:

Assist Prof dr. Athraa Zaidan Hassan استاذ مساعد د. عذراء زيدان حسن

## Target population

Three stage students in department Medical Laboratory Techniques

## Introduction

Adenoviruses most commonly cause respiratory illness; however, depending on the infecting serotype, they may also cause various other illnesses, such as gastroenteritis, conjunctivitis, cystitis (bladder infection), and rash illness. Symptoms of respiratory illness caused by adenovirus infection range from the common cold syndrome to pneumonia, croup, and bronchitis. Young infants and especially patients with

compromised immune systems are more susceptible to severe complications of adenovirus infection. Acute respiratory disease (ARD), which was first recognized among military recruits during World War II, can be caused by adenovirus infections. Adenoviruses were first isolated in human adenoids (tonsils), from which the name is derived. Adenoviruses represent the largest non enveloped viruses, because they are the maximum size able to be transported through the endosome. Adenoviruses are medium sized (90-100 nm), non enveloped icosahedral viruses containing double- stranded DNA.

## Pretest

**Genome of Adenovirus contain the following:-**

**a) dsDNA b) dsRNA c) ssDNA d) ssRNA**

## Scientific Content

### Adenovirus

**Family: Adenoviridae**

**Classification Contain two genera:-**

1- **Masta adenovirus**. Infect the human .

2- **Avia adenovirus** Infect birds.

3- More than 60 serotypes infect human.

4- Adenoviruses are divided into seven Subgroups or species **(A to G)** based on physical, chemical, biological properties.

**-Subgroup A: serotype12, 18 and 31**: highly oncogenic and cause sarcoma when injected into new born hamsters.

**Properties of adenoviruses**

● Composition: DNA(13%), Protein(87%).

● Genome: Linear, double stranded DNA, 26-45 kbp ,

● The surface of its capsid consisting of three major proteins; hexon, penton base and a knobbed fiber .

● Hexon & penton capsomeres are the major components on the surface of the virus particle

- Penton base with toxin-like activity
- Fibers – with type – specific antigens; associated with hemagglutinating activity.
- Adenoviruses are unusually stable to chemical and physical agents and to adverse PH conditions, thus allowing for prolonged survival outside of the body that adenovirus **resistant** Acid , Detergent, Dry environment **while Inactivated** by Heat, Formaldehyde, Bleach.

**Transmission**

Adenoviruses are transmitted by several mechanisms

• **Direct contact,** Adenoviruses causing conjunctivitis are very infectious and spread by direct contamination of the eye.

• **Respiratory droplets** . Respiratory adenoviruses are spread by the respiratory route (aerosol droplet, direct and indirect).

• **Feco-oral route.** Enteric adenoviruses are spread via the fecal-oral route.

**Viral replication:**

1- Adenoviruses attach to surface of the cells by their fibers, then penetrate the cell, and once inside the cell, uncoated the viral DNA.

2- The viral DNA is then transported into the nucleus of the cell and initiates replication cycle.

3- Host cell DNA-dependent RNA polymerase transcribes the early genes leading to formation of functional m RNA.

4- Then the cytoplasm, the early m RNA is translated to nonstructural proteins.

5- In the nucleus , after viral DNA replication, late m RNA is transcribed and then translated into structural virion proteins.

6- This is followed by assembly of virions in the nucleus and release of virions by lysis of the cells, but not by budding.

**Pathogenesis**

Adenoviruses are transmitted mainly by respiratory or feco-oral contact from humans. They infect the conjunctiva or the nasal mucosa. They may multiply in conjunctiva, pharynx, or small intestine, where epithelial cells are infected.

The site of entry generally dictates the type of infection; 2 processes can occur:

These are (a) lytic infection, (b) latent infection.

**(A) Lytic infection:** Adenoviruses infect muco epithelial cells in the respiratory tract, gastrointestinal tract, and conjunctiva or cornea, causing damage of these cells directly(cell lysis ) . After local replication of the virus, viremia follows with subsequent spread to visceral organs. Dissemination occurs more commonly in immunocompromised patients than in the immunocompetent individuals.

**(B) Latent infection:** The adenovirus has unique ability to become latent in lymphoid and other tissues such as adenoids, tonsils, and payer s patches. The exact mechanism of latency of adenovirus in these tissue is not known. These latent infections can be reactivated in patients infected with other agents or in the patients who are immunocompromised.

**Clinical syndrome:** -

Various syndromes are associated with particular serotypes:-

- Respiratory diseases (Phrayngitis and tonsilitis )
- Pharyngioconjunctivitis
- Eye disease (Conjunctivitis)
- Pneumonia: in preschool children
- Gastroenteritis (Gastrointestinal disease)
- Acute hemorrhagic cystitis (bladder infection)
- Cervicitis and urethritis

**Laboratory Diagnosis**

**Specimens**: from throat, eye, urine, feces.

1- Isolation of virus

- Inoculation into cell cultures; human embryonic kidney/ Hela/Hep
- CPE: cell rounding and agglutination into grape like clusters. Others tests: HA, Neutralization, CF.

2- Serology: detection of adenoviral antigens by ELISA, Haemagglutination inhibition test, Neutralization tests and Immunofluorescence for antigen detection in nasopharyngeal/ ocular specimens.

3- Direct detection of Virus particle by Electron microscopy (EM) in stool Sample .

4- PCR indicates adenovirus infection by use type-specific primers can be used to distinguish between different types of adenoviruses.

**Treatment**

There is no antiviral therapy. Limited efficacy of antivirals (Ribavirin ).

**Post test**

**Mention Laboratory Diagnosis of Adenovirus ?**

**References**

1- Review of Medical Microbiology and Immunology. Warren Levinson, 12th May 2012. Mc Graw-Hill (Lange).

2- Jawetz, R., J.L. Melnick, and E.A. Adelberg,( 2019). Review of Medical Microbiology, Twenty-Eighth Edition Edition,.

3- Christopher J. Burrell, ... Frederick A. Murphy, in Fenner and White's Medical Virology (Fifth Edition), 2017

## Title:-

**Parvovirus** **Lecture 16**

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## Target population

**Three stage students in department Medical Laboratory Techniques**

## Introduction

**Parvovirus**, commonly abbreviated to **parvo**, is a genus of the Parvoviridae family linear, non-segmented s**ingle stranded DNA** viruses with an average genome size of 5 kbp. Parvoviruses are some of the smallest viruses found in nature (hence the name, from Latin **parvus** meaning *small*).

## Pretest

**Genome of Parvovirus contain the following:-**

**a) dsDNA b) dsRNA c) ssDNA d) ssRNA**

## Scientific Content

**Properties of Parvoviruses :-**

- Parvoviruses are the smallest DNA.
- Icosahedral, non enveloped particles are 18–26 nm in diameter.
- Virions are extremely resistant to inactivation.
- They are stable between a pH of 3 and 9 and withstand heating at 56°C for 60 minutes, but they can be inactivated by formalin, and oxidizing agents.
- Virions contain two coat proteins ; VP1 and VP2.
- The genome is about 5 kb, linear, single-stranded DNA.
- Virions contain either positive or negative-sense strands. They need help from other viruses or from rapidly dividing host cells in order to replicate.

## Classification:

There are two subfamilies of Parvoviridae :-
**1- Parvovirinae**, which infect vertebrates, which have three genera:

**a) Parvovirus** :- which takes its name from that of the family, and infects only animals and birds;
**b) Dependovirus** :- named for dependence on a helper virus, usually an adenovirus, but occasionally a herpesvirus, to assist in replication.
**c) Erythrovirus** :- which has only one member, known as B19, the only parvovirus causing significant disease in humans; Erythema infectiosum, Fetal infections and Aplastic crisis .

**2- Densovirinae** which infect insects.

**Transmission**:

1- Respiratory route.
2- Transmitted by blood transfusions or by infected blood products.
3- Vertically from mother to fetus.

**Parvovirus Replication:**

Only primary erythroid progenitors are known to be permissive for B19 infection. The cellular receptor for B19 is blood group P antigen which is expressed on mature erythrocytes, erythroid progenitors, megakaryocytes, endothelial cells, placenta, and fetal liver and heart, which helps explain the narrow tissue tropism of B19 virus.

**Clinical features:**

**1- Erythema infectiosum (Fifth Disease)**

This manifestation is most common illness in children of early school age and occasionally affects adults. Fever and mild constitutional symptoms may accompany the rash, which has a typical “slapped cheek” appearance followed by a maculopapular rash on the trunk and limbs, which may persist for 2 or 3 weeks Joint involvement due to immune complex deposition is a prominent feature in adult cases; joints in the hands and the knees are most frequently affected. The symptoms mimic rheumatoid arthritis. The incubation period is usually 1–2 weeks but may extend to 3 weeks.

**2- Transient Aplastic Crisis:** Parvovirus B19 is the cause of transient aplastic crisis (with very low hemoglobin and disappearance of circulating reticulocytes) that may complicate chronic hemolytic anemia, such as in patients with sickle cell disease,

thalassemia, and acquired hemolytic anemia in adults. Transient aplastic crisis may also occur after bone marrow transplantation.

**3-B19 Infection During Pregnancy (Fetal infection) :** Maternal infection with B19 virus may pose a serious risk to the fetus, resulting in hydrops fetalis and fetal death due to severe anemia. Fetal death occurs most commonly before the 20th week of pregnancy.

**Laboratory Diagnosis:**

Specimen; blood cells, tissue samples, and respiratory secretions.

1- **Polymerase chain reaction (PCR),** in situ hybridization. PCR is the most sensitive assay.

2-**Immunohistochemistry** has been used to detect B19 antigens in fetal tissues and bone marrow.

4-Detection of IgM antibody by **ELISA** indicates a current or recent infection, whereas the much more prolonged presence of IgG is a sign of past infection.

**Treatment and Prevention**:

There is no vaccine against human parvovirus and there is no antiviral drug therapy.

**Post test**

**Q1:- Multiple choice ?**

**1- The only parvovirus causing significant disease in humans is :-**

**a- Dependovirus b- Parvovirus c- Erythrovirus d- non of them**

**2- Virion of parvovirus contain :-**

**a- ss DNA b- ds DNA c- ss RNA d- ds DNA**

# References

1- Review of Medical Microbiology and Immunology. Warren Levinson, 12th May 2012. Mc Graw-Hill (Lange).

2- Jawetz, R., J.L. Melnick, and E.A. Adelberg,( 2019). Review of Medical Microbiology, Twenty-Eighth Edition Edition,.

3- Christopher J. Burrell, ... Frederick A. Murphy, in Fenner and White's Medical Virology (Fifth Edition), 2017

## Title:-

**Arbovirus** **Lecture 17**

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## Target population

**Three stage students in department Medical Laboratory Techniques**

## Introduction

**Arboviruses** is a term used to describe a group of RNA viruses transmitted to humans by blood-sucking arthropods from one vertebrate host to another. There are many strains of arbovirus.

The viruses range in severity from no symptoms to mild flu-like symptoms to very severe symptoms. Avoiding insect bites is key to preventing these nasty viral infections. Avoiding insect bites is key to preventing these nasty viral infections.

Insects that can infect humans with arboviruses include fleas, ticks, gnats, and mosquitoes. There are over 130 different arboviruses that affect humans.

## Pretest

**Define Arboviruses?**

# Scientific Content

**General properties The arboviruses share some common biological**

1- They can multiply in the tissues of the arthropod without evidence of disease or damage

2- The vector acquires a lifelong infection through the ingestion of blood from a viremic vertebrate.

3- All arboviruses have an RNA genome, and most have a lipid-containing envelope.

4- All members produce fatal encephalitis in suckling mice after intracerebral inoculation

5- They possess haemagglutinin and agglutinate erythrocytes of goose or day-old chicks

6- They can be grown in tissue cultures of primary cells like chick embryo fibroblasts or continuous cell lines like vero, and in cultures of appropriate insect tissues

7- They may also be isolated in the yolk sac or CAM of chick embryo

8. In general, arboviruses are readily inactivated at room temperature and by bile salts, ether or sodium deoxycholate and other lipid solvents.

**Common types of Arbovirus**

There are many types of arboviruses. The different types of arbovirus are broken down into specific genera.

The three main genera for arboviruses that cause infections in humans are as follows:

1- flavivirus
2-togavirus
3- bunyavirus

Types of flavivirus include the following:

- Yellow fever
- West Nile virus
- Zika virus
- dengue fever

- Japanese encephalitis

**Types of togavirus include the following:**

- Ross River virus
- Eastern equine virus
- Western equine virus

**Types of bunyavirus include the following:**

- California encephalitis
- La Crosse virus
- Jamestown Canyon virus

**Transmission**

The arboviruses spread mainly through insect bites. The most common insect that spreads arboviruses is the mosquito. However, other arthropods such as ticks, fleas, and gnats can also spread these diseases if they bite a human. While insect bites are the most common way arboviruses are transmitted, the viruses can also spread through blood transfusion , organ transplant , sexual contact, pregnancy and childbirth from mother to child.

**Pathogenesis**

→When an infected vector bites a suitable host, the virus is injected into the capillary circulation.

→Virus comes in contact with susceptible target cells such as endothelial cells of capillaries, monocytes, macrophages and cells of RES.

→After replication in endothelial cells and RE cells, a secondary viraemia usually results leading to infection of target organs such as brain, skin, musculature and liver, depending on the tissue tropism.

→The virus reaches the brain by infecting small blood vessels of the brain or choroid plexus.

**Clinical feature**

Most infections caused by arboviruses asymptomatic .however , symptom when present can range from a mild flu-like illness to encephalitis, a potentially life-threatening inflammation and swelling in the brain.

The clinical characteristics and symptoms are divided into two subgroups:-

**1- Neuroinvasive diseases** indicating that the disease can infect the nervous system, often cause meningitis or encephalitis. Symptoms of neuroinvasive arboviruses include the sudden onset of fever , headache , stiff neck, muscle pain, confusion or disorientation, weakness in the arms and legs, seizures.

**2- Non-neuroinvasive diseases** in this disease arboviruses differ slightly in their symptoms. The nervous system is not affected, so they do not typically cause altered mental state, such as confusion or seizures.

non-neuroinvasive arboviruses can cause a fever in addition to headache , muscle aches , upset stomach, joint pain , nausea, vomiting or diarrhea, rash.

**Laboratory Diagnosis of Arbovirus**

**Specimen:** Blood, CSF (Cerebrospinal fluid) and Brain may be used for isolation of virus. All Arboviruses are viremia – blood is collected during the acute phase of the disease. CSF is useful in encephalitis cases but the best specimen is the brain.

Diagnosis may be established by virus isolation or serology.

**Isolation of the virus :**

a) Suckling mice – specimens are inoculated intracerebrally into suckling mice. The animal may develop fatal encephalitis.

b) Tissue culture – Arboviruses may also be isolated in tissue cultures – Vero, BHK-21 and mosquito cell lines are inoculated with specimens. The growth of virus in cell cultures is identified by immunofluorescence, haemagglutination inhibition, complement fixation, ELISA or neutralization tests.

**Serology:** Using ELISA, serotype-specific IgM antibody may be detected in patient serum within 1-3 days after the onset of illness.

**Prevention**

While effective vaccines are available for some arboviruses, including Japanese encephalitis and yellow fever, there is not a vaccine for all arboviruses. Many other vaccines for arboviruses are currently being developed, however. The best way to prevent arboviral infections is by preventing insect bites particularly in areas that have high incidences of arboviruses.

**Post test**

**Q1:- Multiple choice ?**

**1- dengue fever belong to the :-**

a- togavirus b- b- bunyavirus c- flavivirus d- Non of them e- All of them

**2- Susceptible target cells of Arboviruses are :-**

a- Endothelial cells of capillaries b- monocytes c- macrophages d- cells of RES. e- All of them

**References**

1- Review of Medical Microbiology and Immunology. Warren Levinson, 12th May 2012. Mc Graw-Hill (Lange).

2- Jawetz, R., J.L. Melnick, and E.A. Adelberg,( 2019). Review of Medical Microbiology, Twenty-Eighth Edition Edition,.

3- Christopher J. Burrell, ... Frederick A. Murphy, in Fenner and White's Medical Virology (Fifth Edition), 2017

**Title:-**

**Oncogenic viruses (Human cancer viruses)** **Lecture 18**

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## Target population

**Three stage students in department Medical Laboratory Techniques**

## Introduction

**Cell growth**: is the cell proliferation (the increase in cell numbers that occurs through repeated cell division).

• Cell growth is regulated by **two groups of regulatory genes:**

**A. Proto-oncogenes (cellular oncogene, c-onc)**

Are normal genes which control cell proliferation, but which have the potential to contribute to cancer development if their expression is altered (changed into oncogenes). So Oncogenes are genes that cause cancer.

**B- Tumor Suppressor Genes** include genes that inhibit cell growth , fixing broken DNA or causing a cell to die. Examples: P53, Rb (retinoblastoma ) .

An important difference between oncogenes and tumor suppressor genes is that oncogenes result from the activation **(turning on) of proto-oncogenes**, but tumor suppressor genes cause cancer when they are inactivated **(turned off).**

In normal cells, oncogenes are ‘‘switched off’’or down-regulated by antioncogeneproteins.

An **oncovirus** is a virus that can cause cancer.

• It refers to any virus with a DNA or RNA genome causing cancer and also called "tumor virus" or "cancer virus".

• Most viruses are non-transforming - however, they may play a role in reducing the host cell’s ability to inhibit apoptosis.

## Pretest

**Define oncogenic viruses ?**

## Scientific Content

A virus that is able to cause cancer is known as an **oncogenic virus**. Evidence that a virus is oncogenic includes the regular presence in the tumor cells of virus DNA, which might be all or a part of the virus is possible that the virus is just one of a number of carcinogenic factors that can give rise to these cancers.

At least **15-20%** of all human tumors worldwide have a viral cause. The viruses that have been strongly associated with human cancers. Viruses are etiologic factors in the development of several types of human tumors, including two of great significance worldwide cervical cancer and liver cancer. They include **human papillomaviruses** (HPVs), **Epstein-Barr virus** (EBV), **human herpesvirus 8**, **hepatitis B virus**, **hepatitis C virus**, and two **human retroviruses** plus several **candidate human cancer** viruses. Many viruses can cause tumors in animals, either as a consequence of natural infection or after experimental inoculation.

**CLASSES OF ONCOGENIC VIRUSES:** There are two classes of tumor viruses:

- **DNA tumor viruses**
- **RNA tumor viruses, the latter also being referred to as Retroviruses.**

**DNA tumor viruses :-**

1- **Papovaviridae** include human papilloma virus causes uterine (cervical) cancer.

2- **polyomaviridae** include JK,BK causes solid tumor in rodents and Merkel Cell Polyomavirus cause Merkel Cell Carcinoma (rare skin cancer).

**3- Herpesviridae include :-**

a) EBV infection increases the risk of Burkitt lymphoma, Nasopharyngeal carcinoma and some types of Hodgkin's and non-Hodgkin's lymphoma also stomach cancer.
b) Kaposi's sarcoma-associated herpesvirus (KSHV or HHV-8) is associated with Kaposi's sarcoma, a type of skin cancer.
c) Human cytomegalovirus (CMV or HHV-5) is associated with mucoepidermoid carcinoma and possibly other malignancies.

4- **Hepadnaviridae** include Hepatitis B virus causes hepatocellular carcinoma.

5- **Adenoviridae** include adenovirus causes various solid tumor in rodents .

6- **Poxviridae** include Smallpox; cowpox causes various solid tumor.

**RNA tumor Viruses**

**1-Retroviridae** include Human T-cell leukemia virus (HTLV-1; HTLV-2) which causes Adult T-cell leukemia, Lymphoma.

**2-Flaviviridae** include Hepatitis C Virus causes Hepatocellular carcinoma.

**General Features of Viral Carcinogenesis**

1- Viruses can cause cancer in animals and humans.

2- Tumor viruses frequently establish persistent infections in natural host.

3- Viruses are seldom complete carcinogens.

1- Host factors are important determinants of virus-induced tumorigenesis

5. Virus infections are more common than virus-related tumor formation.

6. Long latent periods usually elapse between initial virus infection and tumor appearance.

7- Viral strains may differ in oncogenic potential.
8- Viruses may be either direct- or indirect-acting carcinogenic agents.
9- Oncogenic viruses modulate growth control pathways in cells.
10- Animal models may reveal mechanisms of viral carcinogenesis.

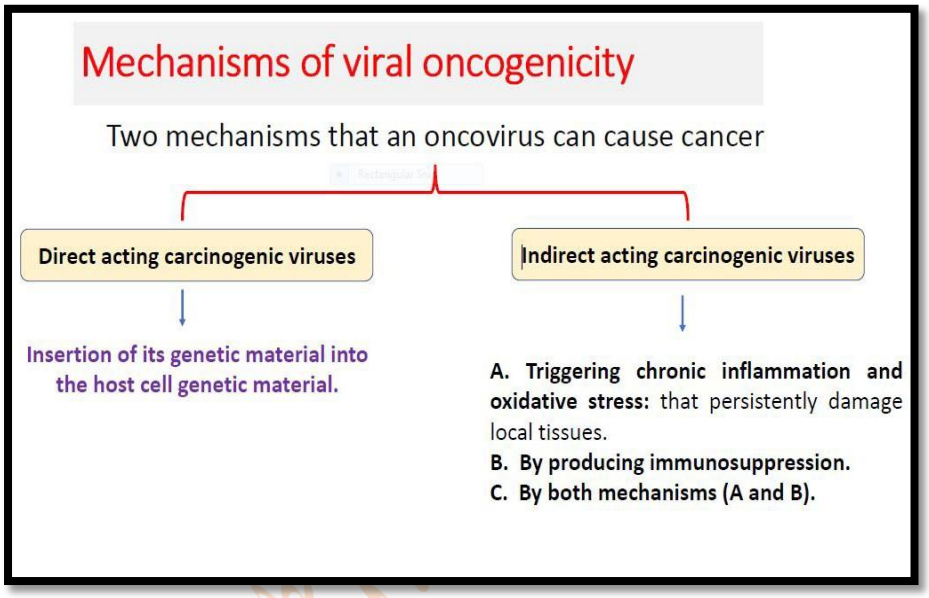
## How do viruses cause cancer?

Viruses typically initiate cancer development by suppressing the host's immune system, causing inflammation over a long period of time, or by altering host genes. Most virus-induced cancers develop after a long period of persistent infection with an oncogenic virus; for adult T cell leukaemia this period is exceptionally long (around 60 years). The virus infections persist in their hosts in spite of immune responses, such as the production of virus-specific antibodies.

As cancer develops in only small percentages of virus-infected hosts it is clear that the virus infections alone do not cause cancer. several factors influence the progression from viral infection to cancer development. These factors include host's genetic makeup, mutation occurrence, exposure to cancer causing agents, and immune impairment.

## Mechanisms of Action by Human Cancer Viruses

Tumor viruses mediate changes in cell behavior by means of a limited amount of genetic information. There are two general patterns by which this is accomplished: The tumor virus introduces a new "**transforming gene**" into the cell (**direct-acting**), or the virus alters the expression of a preexisting cellular gene or genes **(indirect-acting).** In either case, the cell loses control of normal regulation of growth processes. DNA repair pathways are frequently affected, leading to genetic instability and a mutagenic phenotype.




## Papillomavirus-linked cancers

Cervical carcinoma is the third most common cancer in women, with approximately half a million new cases and 280 000 deaths in the world each year. Most, if not all, of these cancers result from infection with a papillomavirus. The papillomaviruses are small DNA viruses of mammals and birds .

They enter the body through small abrasions and infect keratin-making cells (keratinocytes) in skin or a mucous membrane. Each HPV type infects a preferred site, such as the hands or the genitals, and infection may result in a benign wart (papilloma) or a carcinoma.

Most papillomavirus infections do not become persistent, but in a minority of hosts the infection is not cleared by the host's immune response. In individuals who harbour persistent infection there is a small risk of cancer developing. This risk is associated

with about 15 of the HPV types; these '**high-risk**' types include **HPV-16 and 18**. Infection with other HPV types that infect the genitals (Warts) carries little or no risk of cancer; these '**low-risk**' HPV types include **HPV-6 and 11.**

**Human Retroviruses**

The human T-lymphotropic (HTLV) group of retroviruses has probably existed in humans for thousands of years. HTLV-1 has been established as the causative agent of **adult T cell leukemia-lymphomas (ATL**) as well as a nervous system degenerative disorder called tropical spastic Para paresis. It does not carry an oncogene. A related human virus, HTLV-2, has been isolated and associated with Some cases of **hairy cell leukemia**.

Transmission of HTLV-1 seems to involve cell-associated virus. Mother-to-child transmission via breast feeding is an important mode. Such early-life infections are associated with the greatest risk of ATL. Blood transfusion is an effective means of transmission, as are sharing blood-contaminated needles (drug abusers) and sexual intercourse.

**Damage to immune defenses**

Interactions between cell proteins and proteins produced by oncogenic viruses can lead to breakdown of immune defenses that may allow the development of a cancer. Papillomavirus proteins interfere with apoptosis, and hence prevent the death of virus-infected cells.

**Post test**

**Q1:- Multiple choice ?**

**1- Human cytomegalovirus (CMV or HHV-5) is associated with :- :-**

a- mucoepidermoid carcinoma b- Kaposis carcinoma c- hairy cell leukemia

d- Burkitt lymphoma

**2 High-risk types of HPV is associated with - :-**

a- Stomach cancer b-Warts c- cervical carcinoma d- Hodgkin's lymphoma

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1- Review of Medical Microbiology and Immunology. Warren Levinson, 12th May 2012. Mc Graw-Hill (Lange).

2- Jawetz, R., J.L. Melnick, and E.A. Adelberg,( 2019). Review of Medical Microbiology, Twenty-Eighth Edition Edition,.

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## Title:-

**Bacteriophages** **Lecture 19**

## Name of the instructor:

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## Target population

**Three stage students in department Medical Laboratory Techniques**

## Introduction

**Bacteriophages are viruses that infect bacteria.** Replicating within the bacterial cell therefore they are obligate intracellular parasites that multiply inside bacteria by making use of some or all of the host biosynthetic machinery. The term is commonly used in its shortened form, phage. Bacteriophages are much smaller than the bacteria

they destroy . Infection with bacteriophages is restricted to particular strains within a single bacterial species. Phages are ubiquitous and can be found in all reservoirs populated by bacterial hosts, such as soil or the intestines of animals. One of the densest natural sources for phages and other viruses is sea water. They occur widely in nature and can readily be isolated from feces and sewage. There are at least 12 distinct groups of bacteriophages, which are very diverse structurally and genetically.

Typical phages have hollow heads (where the phage DNA or RNA is stored) and tunnel tails, the tips of which have the ability to bind to specific molecules on the surface of their target bacteria. The viral DNA is then
injected through the tail into the host cell, where it directs the production of progeny phages often over a hundred in half an hour. These "young" phages burst from the host cell (killing it) and infect more bacteria.

## Pretest

**Define Bacteriophages ?**

## Scientific Content

**Composition:**

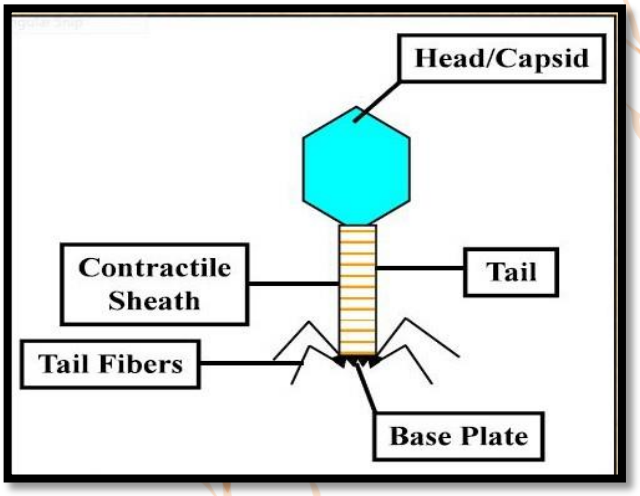
Depending upon the phage, the nucleic acid can be either **DNA or RNA** but not both. The nucleic acids of phages often contain unusual or modified bases, which protect phage nucleic acid from nucleases that break down host nucleic acids during phage infection. Simple phages may have only 3-5 genes while complex phages may have over 100 genes**.** The phages majority contain **double strand DNA (dsDNA),** while there are small phage groups with **ssRNA, dsRNA, or ssDNA.** There are three morphological forms of phages: filamentous phages, isosahedral phages without tails, phages with tails, and even several phages with a lipid-containing envelope or contain lipids in the particle shell.

**Structure of bacteriophages**

- **Size:-** Most phages range in size from 24-200 nm in length. **T4** is among the largest phages; it is approximately 200 nm long and 80-100 nm wide.

● **Head or capsid** :- All phages contain a **head structure,** which can vary in size and shape. Some are icosahedral (20 sides) others are filamentous. The head or capsid is composed of many copies of one or more different proteins. Inside the head is found the nucleic acid. The head acts as the protective covering for the nucleic acid.

● **Tail:-** Some phages have tails attached to the phage head. The tail is a hollow tube through which the nucleic acid passes during infection. T4 tail is surrounded by a contractile sheath, which contracts during infection of the bacterium. At the end of the tail, phages like T4 have a base plate and one or more tail fibers attached to it. The base plate and tail fibers are involved in the binding of the phage to the bacterial cell. Not all phages have base plates and tail fibers.




**Bacteriophage Replication Cycle**

All known bacteriophages can be divided into **two groups** according to **the type of infection** :-

One group is characterized by a **lytic infection** and the other is represented by **a lysogenic**, or **temperate**.

**1- Lytic or virulent phages** are phages, which multiply in bacteria and kill the cell by lysis at the end of the life cycle. Soon after the nucleic acid is injected, the phage cycle is said to be in **eclipse period**. During the eclipse phase, no infectious phage particles can be found either inside or outside the bacterial cell. Eclipse phase represents the interval between the entry of phage nucleic acid into bacterial cell and release of mature phage from the infected cell occurs. The phage nucleic acid takes over the host biosynthetic machinery and phage specified m-RNA's and proteins are

made. Nucleic acid is then packaged inside the head and then tail is added to the head. The assembly of phage components into mature infective phage particle is known as maturation. In Lysis and Release Phase the bacteria begin to lyse due to the accumulation of the phage lysis protein (holins and endolysins) and intracellular phage are released into the medium.

**2- Lysogenic or temperate phages**

Temperate phage has the ability to enter a lysogenic cycle and become a dormant state in the cell, in which the phage DNA is integrated into the host genome. The DNA is replicated along with the host genome. This integrated state of phage DNA is termed **prophage**. This process is known as lysogeny and the bacteria harboring prophage are called **lysogenic bacteria.** Since the prophage contains genes, it can confer new properties to the bacteria. Such transition of viral DNA could take place through several generations of bacterium without major metabolic consequences for it. Eventually the phage genes, at certain conditions impeding the bacterium state, will revert to the lytic cycle, leading to release of fully assembled phages.

Anytime a lysogenic bacterium is exposed to adverse conditions, the lysogenic state can be terminated. This process is called **induction**. Conditions which favor the termination of the lysogenic state include: desiccation, exposure to UV or ionizing radiation, exposure to mutagenic chemicals.

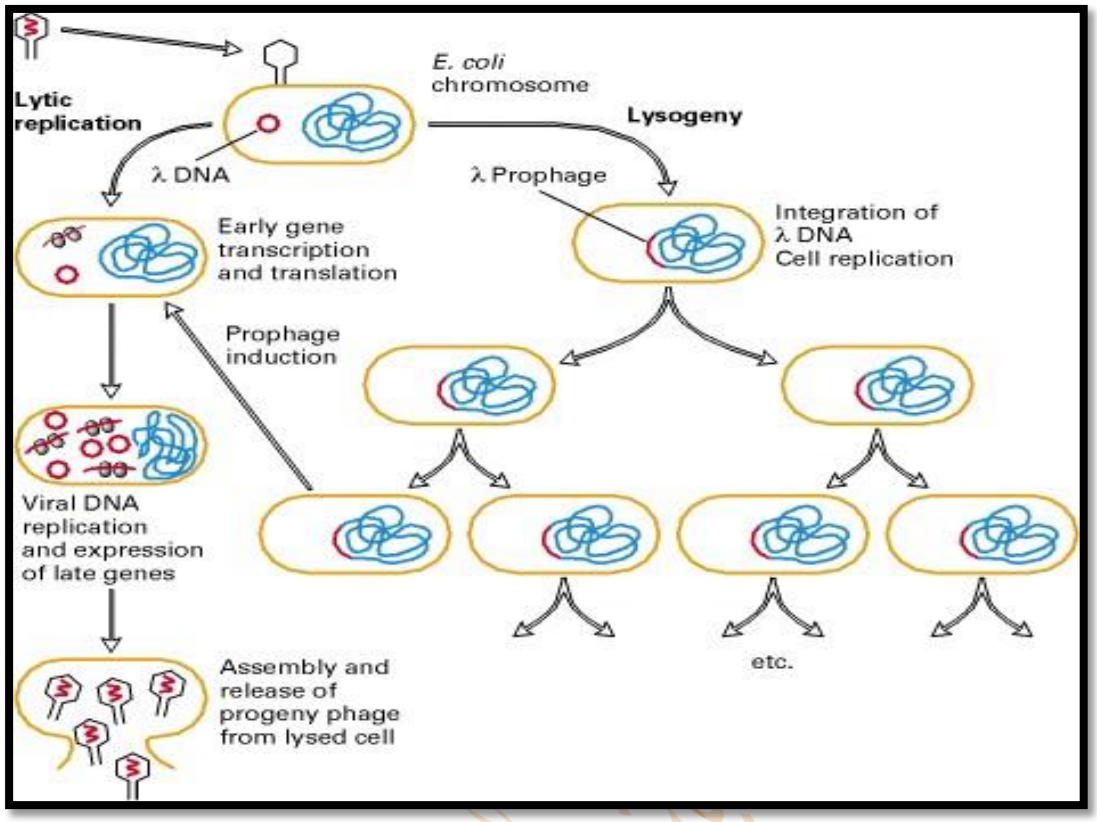
**Significance of lysogenic conversion includes:**

• Lysogenic phages have been shown to carry genes that can modify the Salmonella O antigen. which is one of the major antigens to which the immune response is directed.

• Toxin production by Corynebacterium diphtheriae is mediated by a gene carried by a beta phage. Only those strains that have been converted by lysogeny are pathogenic.

• Clostridium botulinum, a causative agent of food poisoning, makes several different toxins, 2 of which are actually encoded by prophage genomes.

• Lysogenised bacteria are resistant to super infection by same or related phages.This is known as super infection immunity.




**Lytic and Lysogenic Cycle**

## Phage Therapy:

Phage therapy involves clinical treatment of bacterial infections with phages (bacteriophages). The method, which has gained a renewed interest because of increasing frequency of infections by multidrug-resistant bacteria, has potential benefits.

Phages are highly effective in killing their targeted bacteria (their action is bactericidal). Phages may be considered as good alternative for patients allergic to antibiotics.

## Phage therapy benefits

- Phages work against both treatable and antibiotic-resistant bacteria.
- They may be used alone or with antibiotics and other drugs.
- Phages multiply and increase in number by themselves during treatment (only one dose may be needed).
- They only slightly disturb normal "good" bacteria in the body.

- Phages are natural and easy to find.
- They are not harmful (toxic) to the body.
- They are not toxic to animals, plants, and the environment.

**Phage therapy disadvantages**

- Phages are currently difficult to prepare for use in people and animals.
- It's not known what dose or amount of phages should be used.
- It's not known how long phage therapy may take to work.
- It may be difficult to find the exact phage needed to treat an infection.
- Phages may trigger the immune system to overreact or cause an imbalance.
- Some types of phages don't work as well as other kinds to treat bacterial infections.
- There may not be enough kinds of phages to treat all bacterial infections.
- Some phages may cause bacteria to become resistant.

**Post test**

**Q1:-Enumerate phage therapy benefits ?**

**References**

1- Review of Medical Microbiology and Immunology. Warren Levinson, 12th May 2012. Mc Graw-Hill (Lange).

2- Jawetz, R., J.L. Melnick, and E.A. Adelberg,( 2019). Review of Medical Microbiology, Twenty-Eighth Edition Edition,.

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4- M. B. Dion, F. Oechslin, and S. Moineau, "Phage diversity, genomics and phylogeny," Nature Reviews Microbiology, vol. 18, no. 3, pp. 125–138, 2020.

## Title:-

**Antiviral drugs and viral vaccine** **Lecture 20**

## Name of the instructor:

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## Target population

**Three stage students in department Medical Laboratory Techniques**

## Introduction

### Anti-viral Drugs:

**Antiviral drugs** are a class of medication used specifically for treating viral infections. Like antibiotics for bacteria, specific antivirals are used for specific viruses. Designing safe and effective antiviral drugs is difficult, because viruses use the host's cells to replicate. This makes it difficult to find targets for the drug that would interfere with the virus without harming the host organism's cells. Moreover, the major difficulty in developing vaccines and anti-viral drugs is due to viral variation.

**The number of antiviral drugs is very small because:**

1. The virus is obligate intracellular parasite, difficulty in obtaining selective toxicity against virus.
2. Relatively ineffective, because many cycle of viral patients is well. by the time the patients have systemic viral disease .

3. Some virus remain latent in cell e.g. Herpes virus family
4. The emergence of viral drug resistance viral mutates.

## Pretest

**Define Antiviral drugs?**

## Scientific Content

Antiviral drugs are available to treat **only a few viral diseases**. The reason for this is the fact that viral replication is so intimately associated with the host cell that any drug that interferes significantly with viral replication, is likely to be **toxic to the host**. Most of the antiviral drugs now available are designed to help deal with HIV, herpes viruses, the hepatitis B and C viruses, and influenza A and B viruses. Researchers are working to extend the range of antivirals to other families of pathogens.

**Two useful antiviral are:** One way of doing this is to develop nucleotide or nucleoside analogues ( **Nucleotide analogues:**These are **synthetic compounds which resemble nucleosides** , but have an incomplete or abnormal deoxy-ribose /or ribose group) that look like the building blocks of RNA or DNA, but deactivate the enzymes that synthesize the RNA or DNA once the analogue is incorporated. This approach is more commonly associated with the inhibition of reverse transcriptase (RNA to DNA) .

**Stages in virus replication which are possible targets for chemotherapeutic agents:**

- Attachment to host cell
- Uncoating - (Amantadine)
- Synthesis of viral mRNA
- Translation of mRNA (Interferon)
- Replication of viral RNA or DNA (Interferon)
- Maturation of new virus proteins (Protease inhibitors)
- **Assembly**, release :- Protease inhibitors can be developed to prevent the final maturation of viral proteins in viruses that use a polyprotein expression strategy **Rifampicin and Tamiflu.**

**vaccine:-** is a biological preparation that provides active acquired immunity to a particular disease. A vaccine typically contains an agent that **resembles** a disease-causing micro-organism and is often made from **weakened** or **killed** forms of the microbe, its **toxins** or **one of its surface proteins**. Vaccines can be prophylactic or therapeutic (e.g., vaccines against cancer)**.**

Vaccines are very effective on stable viruses, but are of limited use in treating a patient who has already been infected. They are also difficult to successfully deploy against rapidly mutating viruses, such as influenza (the vaccine for which is updated every year) and HIV. Antiviral drugs are particularly useful in these cases.

**Attributes of a good vaccine**

**1.** Ability to elicit the appropriate immune response for the particular pathogen.

**2.** Long term protection.

**3.** Safety.

**4.** Stable.

**5.**Inexpensive.

**Types of Vaccines**

1- Live, attenuated vaccines

2- Inactivated vaccines (killed vaccine)

3- Subunit vaccines

4- Toxoid vaccines

5- DNA vaccines

6- Recombinant vector vaccines

**1- Attenuated Live Vaccines** vaccines contain **live**, **attenuated** microorganisms. Many of these are active viruses that have been cultivated under conditions that **disable their virulent properties**, and become less dangerous organisms to produce a broad immune response. Although **most** attenuated vaccines are **viral**, some are bacterial in nature. **Examples** include the viral diseases measles, rubella, and mumps, and the bacterial disease typhoid.

**2- Killed Viral Vaccines**

Vaccines contain **inactivated** virus, but previously virulent, micro-organisms that have been **destroyed** with chemicals, heat, radiation, or antibiotics **without** destroying the **antigenicity** of the virus. **Examples** are influenza, cholera, hepatitis A, and rabies.

**3- Subunit vaccines**:

viral **proteins** or groups of proteins are used. These proteins can be **purified** directly from viral particles. However this is **expensive**, since it is difficult to prepare virus in large enough quantities for protein purification, and potentially **dangerous** since there is the possibility of contaminating virulent virus.

**4- DNA- Based Vaccines**

genes (DNA) encoding specific viral proteins are injected into an animal (either in muscle or skin). The DNA is then taken up by cells, where it is **transcribed** into **mRNA** which is then **translated to give rise to the viral protein**. This protein is **expressed** on the surface of cells, either alone or in association with MHC molecules. It is **recognized** as a foreign molecule by the immune system, and **elicits an immune response**.

**5- Toxoid Vaccines:**

**For bacteria** that secrete toxins, or harmful chemicals. These vaccines are used when a bacterial toxin is the **main cause** of illness. they can **inactivate** toxins by **treating** them with **formalin** Such “detoxified” toxins, called toxoids, and are **safe for use in vaccines.**

**6-Recombinant vector vaccines**

Immunogenic proteins of virulent organisms may be synthesized artificially by introducing the gene coding for the protein into an expression vector, such as E-coli or yeasts.

## Post test

**Q1:-Enumerate types of viral vaccine ?**

**References**

1- Review of Medical Microbiology and Immunology. Warren Levinson, 12th May 2012. Mc Graw-Hill (Lange).

2- Jawetz, R., J.L. Melnick, and E.A. Adelberg,( 2019). Review of Medical Microbiology, Twenty-Eighth Edition Edition,.

3- Christopher J. Burrell, ... Frederick A. Murphy, in Fenner and White's Medical Virology (Fifth Edition), 2017.

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**Target population:**

**Three stage students in department Medical Laboratory Techniques**

Echinocandins may be used for systemic fungal infections in immunocompromised patients, they inhibit the synthesis of glucan in the cell wall via the enzyme Beta (1-3) glucan synthase:

- Anidulafungin
- Caspofungin
- Micafungin